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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/966,522	09/28/2001	Thomas Krahn	Bayer 10,139.3-KGB	5606
27384	7590	10/18/2007	EXAMINER	
NORRIS, MC LAUGHLIN & MARCUS, PA 875 THIRD AVENUE 18TH FLOOR NEW YORK, NY 10022			DO, PENSEE T	
		ART UNIT	PAPER NUMBER	
		1641		
		MAIL DATE	DELIVERY MODE	
		10/18/2007	PAPER	

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/966,522	KRAHN ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Pensee T. Do	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### **Status**

- 1) Responsive to communication(s) filed on 05 April 2007.
- 2a) This action is **FINAL**.                            2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### **Disposition of Claims**

- 4) Claim(s) 6-43 is/are pending in the application.
- 4a) Of the above claim(s) 6-16 and 24-42 is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 17-23 and 43 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) 6-43 are subject to restriction and/or election requirement.

#### **Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### **Priority under 35 U.S.C. § 119**

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### **Attachment(s)**

- 1) Notice of References Cited (PTO-892)
- 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) Information Disclosure Statement(s) (PTO/SB/08)  
 Paper No(s)/Mail Date \_\_\_\_\_
- 4) Interview Summary (PTO-413)  
 Paper No(s)/Mail Date \_\_\_\_\_
- 5) Notice of Informal Patent Application
- 6) Other: \_\_\_\_\_

## DETAILED ACTION

### ***Amendment Entry & Claims Status***

The amendment filed on April 5, 2007 has been acknowledged and entered.

Claims 17-23 and newly added claim 43 are being examined.

All other claims are withdrawn from further consideration.

### ***Withdrawn Rejection(s)***

Rejection under 112, 1<sup>st</sup> paragraph in the previous office action is withdrawn herein.

### ***New Grounds of Rejection***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-23 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 17 is amended to recite "the fluorescent dye is in a form that permits the fluorescent dye to permeate the membrane". However, the specification fails to support such "form that permits the fluorescent dye to permeate the membrane". The specification only describes fluorescent dye such as bis(1,3-dibutylbarbituric acid) trimethaneoxonol (Dibac4(3)) and a masking dye used is brilliant

Black on page 8. The specification fails to teach any modification of such dyes into a form that permeate the cell membrane.

***Maintained Rejection(s)***

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 17-21, 23 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Wan et al. (Journal of Immunological Methods 162 (1993) pp. 1-7) in view of Cubbage et al. (US 5,582,982).

Wan teaches a method of using fluorescein conjugated E.Coli particles and second dye such as Trypan blue to quench the extracellular fluorescence in the solution. That means Trypan blue absorbs and the extracellular fluorescence which cause the solution to emit non-specific background light in the solution while the fluorescent that absorbs into the cells are being measured. Quenching the extracellular fluorescence thus means reducing non-specific background light in solution. (see abstract, page 3 "Phagocytosis assay" and "results"). Trypan blue is obviously impermeant to the membrane of the cell because it quenches extracellular fluorescence. If it is permeable to the membrane, then it would quench all the fluorescence that absorbs into the cells and there would be no fluorescence left to

detect. Wan also teaches that the concentration of trypan blue require to completely quench extracellular fluorescence was determined by exposing 3 or  $6 \times 10^8$  particles/well to serial dilutions of the dye in a 96-well plate. Complete quenching of the fluorescence was obtained with 250 ug/ml of the dye. Thus, Wan meets the requirement that the non-specific background in solution is reduced by at least 30%, 50% and 70% (claims 18-20). Since Wan teaches a fluorescent dye attached to the cell as in the present invention, such fluorescent dye is inherently permeant to the membrane of the cell and detects a voltage across the membrane of the cell. Since trypan blue can quench or reduce non-specific background, it would inherently be able to perform functions such as to improve the signal to noise ratio by at least 300%.

However, Wan fails to teach these reagents packaged in a kit.

Cubbage teaches a kit comprising a fluorescent probe and a background-reducing compound that diffuses into and onto the biological entity. (see col. 2, line 45-col. 7, line 27).

It would have been obvious to one of ordinary skills in the art package the components taught by Wan into a kit as taught by Cubbage for cost effective or other economic advantages.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Wan et al. (Journal of Immunological Methods 162 (1993) pp. 1-7) in view of Cubbage et al. (US 5,582,982) as applied to claim 17-21, 23 above, and further in view of Van Aken (US 5,489,537).

Wan and Cubbage have been discussed above.

However, Wan and Cubbage fails to teach Brilliant Black as a fluorescent dye.

Van Aken teaches a method and kit for determining the presence or absence of a substance by detection of a colloidal dye associated with agglutinated particles. The colloidal dye is a background-enhancing dye, which reduces non-specific background to enhance optical detection. The background-enhancing dye is a water-soluble dye such as Brilliant Black. (see col. 21, lines 58-67).

It would have been obvious to one of ordinary skills in the art to use Brilliant Black as a masking or quenching dye in the kit for use in the method of Wan and Cubbage because both references teach using quenching or background reducing dye, which reduces background light in assay. Since Brilliant Black is known for enhancing the background in an assay, which uses optical detection, it would motivate one of ordinary skills in the art to use Brilliant Black in assays such as one taught by Wan and Cubbage because both Wan and Cubbage teach using fluorescent label, which is known for producing non-specific background.

#### ***Response to Arguments***

Applicant's arguments filed April 5, 2007 have been fully considered but they are not persuasive.

Regarding the 103 rejection, Applicants argue that because Wan teaches that the fluorescent dyes are attached to the cell, it cannot permeate the cell membrane. Furthermore, the fluorescent dye in Wan is conjugated to E.coli particles and cannot be regarded as fluorescent dye. Wan also expressly teaches that the particles are then taken up by phagocytosis and thus they do not permeate any biological membrane.

Wan also teaches that the fluorescein conjugated E. coli particles were purchased already conjugated. Wan never has unbound fluorescein and never any membrane permeant fluorescent dye.

The claims, as now recited, fail to exclude any extraneous materials such as E.coli particles because they contain opening comprising language. Since Wan teaches using the same fluorescent dyes as those in the present invention, Wan's fluorescent dye are permeant to the cell membrane. The fluorescent dye of the present invention is not modified to be in any special form or structure that would distinguish it from the fluorescent dye in the prior arts. Thus, regardless of how the fluorescent dye is used, i.e. attached to cell or attached to E. coli particle taken up by phagocytosis, it is still a fluorescent dye. The claimed invention is claiming such exact dye.

### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pensee T. Do whose telephone number is 571-272-0819. The examiner can normally be reached on Monday-Friday, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Pensee T. Do  
Patent Examiner  
October 11, 2007

*Long Le* 10/15/07  
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